AD-A138 879 TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT 1/1
REPELLENTS AI3-3835..(U) ARMY ENVIRONMENTAL HYGIENE
AGENCY ABERDEEN PROVING GROUND MD J V WADE ET AL.
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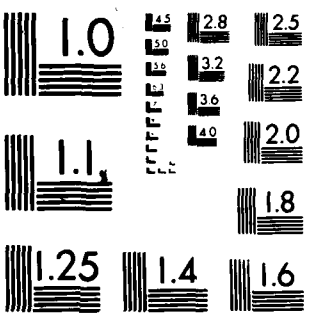

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UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38352a, AI3-38354a, AI3-38355a,
AI3-38357a, AI3-38360a, AND AI3-38361a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0371-84, 75-51-0372-84,
75-51-0373-84, 75-51-0374-84, 75-51-0376-84,
AND 75-51-0377-84
MAY 1982 - NOVEMBER 1983

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REPORT DOCUMENTATION PAGE

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1. REPORT NUMBER: 75-51-0371-0374, 0376-0377-84	2. GOVT ACCESSION NO.
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE *(and Subtitle)*: Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a, US Department of Agriculture Proprietary Chemicals, Study No. 75-51-0371-84 thru 75-51-0374-84 and 75-51-0376-84 and 75-51-0377-84, May 82 - Nov 83	5. TYPE OF REPORT & PERIOD COVERED: Final, May 1982 - November 1983
	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s): John V. Wade, DVM, CPT(P), VC John G. Harvey	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Commander US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS: Commander US Army Health Services Command Ft Sam Houston, TX 78234	12. REPORT DATE: May 1982 - November 1983
	13. NUMBER OF PAGES: 8
14. MONITORING AGENCY NAME & ADDRESS *(if different from Controlling Office)*	15. SECURITY CLASS. *(of this report)*: Unclassified
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT *(of this Report)*

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17. DISTRIBUTION STATEMENT *(of the abstract entered in Block 20, if different from Report)*

18. SUPPLEMENTARY NOTES

19. KEY WORDS *(Continue on reverse side if necessary and identify by block number)*

USDA Proprietary Chemicals	AI3-38360a	Photochemical Irritation
AI3-38352a	AI3-38361a	Guinea Pig Sensitization
AI3-38354a	Skin Irritation	Topical Hazard Evaluation
AI3-38355a	Eye Irritation	Program
AI3-38357a	ALD	

20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

Chemical AI3-38352a produced mild irritation of the intact skin and of the skin surrounding an abrasion. Chemicals AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a produced no primary irritation of the intact skin and no more than mild irritation of the skin surrounding an abrasion. Chemicals AI3-38357a and AI3-38360a were noninjurious to the eye. Chemical AI3-38352a produced mild injury to the cornea. Chemicals AI3-38354a, AI3-38355a, and AI3-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. These chemicals did not elicit a photochemical irritation reaction or produce sensitization. All chemicals were relatively nontoxic by ingestion.

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U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

CPT(P) Wade/cvc/AUTOVON
584-3980

REPLY TO
ATTENTION OF

HSHB-OT/WP

1 MAR 1984

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI38360a, and AI3-38361a, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, and 75-51-0377-84, May 1982 - November 1983

Executive Summary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20307

EXECUTIVE SUMMARY

The purpose, essential findings, and major recommendations of the inclosed report follow:

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of candidate insect repellents AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI38360a, and AI3-38361a by means of laboratory studies using New Zealand White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs.

b. Essential Findings. Chemical AI3-38352a produced mild irritation of the intact skin and the skin surrounding an abrasion. The other chemicals produced no primary irritation of the intact skin and no greater than mild primary irritation of the skin surrounding an abrasion. Chemicals AI3-38357a and AI3-38360a were noninjurious to the eye. Chemical AI3-38352a produced mild injury to the cornea. Chemicals AI3-38354a, AI3-38355a, and AI3-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. These chemicals did not illicit a photochemical irritation reaction or produce sensitization. All six were relatively nontoxic by ingestion.

c. Major Recommendations. Recommend that chemicals AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a be approved for further entomological testing as candidate insect repellents.

FOR THE COMMANDER:

Walter G. Pitt, Lt, MSC
for JOEL C. GAYDOS, M.D.
Colonel, MC
Director, Occupational and Environmental Health

1 Incl
as (5 cy)

CF:
HQDA (DASG-PSP) wo incl
Cdr, HSC (HSPA-P)
Comdt, AHS (HSHA-P)
Dir, Advisory Cen on TOX, NRC (2 cy)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region
Cdr, USAMRDC, [SGRD-DPM/LTC(P) Reinert]

A-1

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

REPLY TO ATTENTION OF
HSHB-OT/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, AND AI3-38361a US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS STUDY NOS. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, AND 75-51-0377-84 MAY 1982 - NOVEMBER 1983

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 29 April 1982.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administrations; titled Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Standing Operating Procedures, US Army Environmental Hygiene Agency (USAEHA), 1981.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of candidate insect repellents AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a, US Department of Agriculture (USDA) Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluations of candidate insect repellents AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a, USDA Proprietary Chemicals were conducted by this Agency using New Zealand White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs. A tabular presentation of animal toxicity data developed at this Agency follows: *†

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 80-23, revised 1978.
† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, 75-51-0377-84, May 82 - Nov 83

TABLE. PRESENTATION OF DATA.

TEST	RESULTS		INTERPRETATION
SKIN IRRITATION STUDIES Rabbits			
Single 24-hour application to intact and abraded skin of New Zealand White rabbits. 0.5 mL technical grade chemical applied to each of six rabbits.	Chemicals AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a and AI3-38361a produced no primary irritation of the intact skin and no greater than mild irritation of the skin surrounding an abrasion.		USAEHA Category I (ref Appendix A)
	Chemical AI3-38352a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion.		USAEHA Category II (ref Appendix A)
EYE IRRITATION STUDIES Rabbits			
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute, 25 seconds after application.	Chemical AI3-38357a and AI3-38360a were noninjurious to the eyes of rabbits.		USAEHA Category A (ref Appendix A)
	Chemical AI3-38352a produced mild injury to the cornea.		USAEHA Category B (ref Appendix A)
	Chemicals AI3-38354a, AI3-38355a, and AI3-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva.		USAEHA Category C (ref Appendix A)
APPROXIMATE LETHAL DOSE Oral			
Rats (Male) - No Diluent	AI3-38352a	$\geq$5,000 mg/kg	These chemicals were relatively nontoxic by ingestion.
	AI3-38354a	$\geq$3,333 mg/kg	
	AI3-38355a	3,333 mg/kg	
	AI3-38357a	$\geq$2,222 mg/kg	
	AI3-38360a	$\geq$3,333 mg/kg	
	AI3-38361a	$\geq$3,333 mg/kg	

Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, 75-51-0377-84, May 82 - Nov 83

TEST	RESULTS	INTERPRETATION
PHOTOCHEMICAL SKIN IRRITATION STUDIES Rabbits		
A single 0.05 mL application of a 25% (w/v) solution of each test chemical and of 10% (wv) Oil of Bergamot (positive control) in 95% ethyl alcohol was applied to the intact skin of six rabbits. Five minutes after application the rabbits were exposed to ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm.	A 25% solution of chemical AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a did not cause a photochemical irritation reaction.	The tested chemicals did not cause a photochemical irritation reaction under test conditions and are not expected to cause a photochemical irritation reaction in humans.
Control Following UV exposures of the rabbits, 0.05 mL of the test chemical, positive control (Oil of Bergamot) and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48, and 78 hours.	Positive control application and irradiation caused a greater irritant effect than in unirradiated skin areas.	
SENSITIZATION STUDIES Guinea Pigs (Male)		
Intradermal (ID) injections of 0.1 mL of a minimally irritating concentration of each tested chemical or of dinitrochlorobenzene (DNCB)† in a mixture containing 1 volume of propylene glycol and 29 volumes of saline. Ten guinea pigs were given 10 sensitizing doses over a 3-week period. After a 2-week rest, they were challenged with an ID injection of the test chemical.	Challenge doses of chemicals AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a did not produce sensitizing reactions.	These chemicals did not produce sensitizing reactions under test conditions and are not expected to cause sensitization in humans.

† A known skin sensitizer

Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, 75-51-0377-84, May 82 - Nov 83

TEST	RESULTS	INTERPRETATION
Ten positive control guinea pigs were sensitized over a 3-week period. After a 2-week rest, they were challenged with ID injections of DNCB.	Challenge doses of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	DNCB produced a marked reaction indicating that these guinea pigs respond to sensitizing agents.

5. CONCLUSION. Chemical AI3-38352a produced mild irritation of the intact skin and of the skin surrounding an abrasion. Chemicals AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a produced no primary irritation of the intact skin and no more than mild irritation of the skin surrounding an abrasion. Chemicals AI3-38357a and AI3-38360a were noninjurious to the eye. Chemical AI3-38352a produced mild injury to the cornea. Chemicals AI3-38354a, AI3-38355a, and AI3-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. These chemicals did not elicit a photochemical irritation reaction or produce sensitization. All six were relatively nontoxic by ingestion. These studies were monitored by the Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATIONS. Recommend USDA Proprietary Chemicals AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a and AI3-38361a be approved for further testing as candidate insect repellents (under the provisions of the Memorandum of Understanding, paragraph 1b, this report).

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APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, 75-51-0377-84, May 82 - Nov 83

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following:

a. These studies were conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations(CFR), 1983 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

(3) Proposed Rule, Pesticide Programs; Good Laboratory Practice Standards; Final Rule, 48 Federal Register (FR) 53946-53969, 29 November 1983.

b. Facilities were inspected during its operational phase to ensure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting these studies.

PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office


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